Claims

1. A modified mevalonate kinase which exhibits a sensitivity to feedback inhibition which is reduced in comparison to the corresponding non-modified mevalonate kinase wherein

(i) the amino acid sequence of the modified mevalonate kinase contains at least one mutation when compared with the amino acid sequence of the corresponding non-modified mevalonate kinase and

(ii) the at least one mutation is at one or more amino acid positions selected from the group consisting of amino acid positions corresponding to positions 17, 47, 93, 94, 132, 167, 169, 204, and 266 of the amino acid sequence of *Paracoccus zeaxanthinifaciens* mevalonate kinase as shown in SEQ ID NO:1.

2. A modified mevalonate kinase according to claim 1 wherein said feedback inhibition is feedback inhibition by farnesyl diphosphate or geranylgeranyl diphosphate.

3. A modified mevalonate kinase according to claim 1 or 2 wherein the modified mevalonate kinase exhibits a feedback resistance of at least 10% in comparison to the corresponding non-modified mevalonate kinase.

4. A modified mevalonate kinase according to any one of claims 1 to 3 wherein the mutation is an amino acid substitution.

5. A modified mevalonate kinase according to any one of claims 1 to 4 wherein the modified mevalonate kinase contains two amino acid substitutions when compared with the amino acid sequence of the corresponding non-modified mevalonate kinase.

6. A modified mevalonate kinase according to any one of claims 1 to 5 wherein the modified mevalonate kinase contains 3 amino acid substitutions when compared with the amino acid sequence of the corresponding non-modified mevalonate kinase.

7. A modified mevalonate kinase according to any one of claims 1 to 6 wherein the modified mevalonate kinase contains 4 amino acid substitutions when compared with the amino acid sequence of the corresponding non-modified mevalonate kinase.

8. A modified mevalonate kinase according to any one of claims 1 to 7 wherein the modified mevalonate kinase contains a substitution when compared with the amino acid sequence of the corresponding non-modified mevalonate kinase wherein the substitution

is at the amino acid position corresponding to amino acid position 17 of the sequence as shown in SEQ ID NO:1.

9. A modified mevalonate kinase according to claim 8 wherein the substitution at the amino acid position corresponding to position 17 of the sequence as shown in SEQ ID NO:1 consists of the replacement of isoleucine with threonine.

10. A modified mevalonate kinase according to any one of claims 1 to 9 wherein the amino acid sequence of the corresponding non-modified mevalonate kinase is selected from the group consisting of the amino acid sequences as shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 30.

11. A polynucleotide comprising a nucleotide sequence which codes for a modified mevalonate kinase according to any one of claims 1 to 10.

12. A polynucleotide according to claim 11 wherein the nucleotide sequence which codes for a modified mevalonate kinase according to any one of claims 1 to 10 is selected from the group consisting of the nucleotide sequences SEQ ID NOs: 32 and 33.

13. A vector or plasmid comprising a polynucleotide according to claim 11 or 12.

14. A vector or plasmid according to claim 13 further comprising at least one marker gene.

15. A host cell comprising the vector or plasmid according to claim 13 or 14.

16. A host cell according to claim 15 which is an *E. coli* or *Paracoccus zeaxanthinifaciens* or *Rhodobacter* or *Saccharomyces cerevisiae* cell.

17. A method for producing an isoprenoid compound comprising:

(a) culturing the host cell according to claim 15 or 16 in a suitable medium; and

(b) optionally separating the isoprenoid compound from the medium.

18. A method according to claim 17 wherein the isoprenoid compound is coenzyme Q10.

19. A method for producing a modified mevalonate kinase according to any one of claims 1 to 10 comprising:

(a) culturing a population of host cells according to claim 15 or 16 in a suitable medium; and

(b) optionally recovering the modified mevalonate kinase from the cells or from the medium.

20. A method for the preparation of a mevalonate kinase having reduced sensitivity to feedback inhibition, comprising the following steps:

(a) providing a polynucleotide encoding a first mevalonate kinase which exhibits sensitivity to feedback inhibition;

(b) introducing one or more mutations into the polynucleotide sequence such that the mutated polynucleotide sequence encodes a second mevalonate kinase which contains at least one amino acid mutation when compared to the first mevalonate kinase wherein the at least one amino acid mutation is at one or more amino acid positions selected from the group consisting of amino acid positions corresponding to positions 17, 47, 93, 94, 132, 167, 169, 204, and 266 of the amino acid sequence as shown in SEQ ID NO:1;

(c) optionally inserting the mutated polynucleotide in a vector or plasmid;

(d) introducing the polynucleotide or the vector or plasmid into a suitable host cell; and

(e) culturing the host cell under conditions that allow expression of the modified mevalonate kinase.

21. The use of a modified mevalonate kinase according to any one of claims 1 to 10 or a polynucleotide according to claim 11 or 12 for the manufacture of a medicament for the treatment of a disorder associated with decreased activity of mevalonate kinase.

22. The use of claim 21 wherein the disorder associated with decreased activity of mevalonate kinase is selected from the group consisting of mevalonic aciduria, and hyperimmunoglobulinemia D and periodic fever syndrome.

23. The use of a modified mevalonate kinase according to any one of claims 1 to 10 or a polynucleotide according to claim 11 or 12 for determining the concentration of mevalonate in biological fluids.

24. The use of a modified mevalonate kinase according to any one of claims 1 to 10 or a polynucleotide according to claim 11 or 12 for increasing the production of an isoprenoid compound.

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